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<110> Baron, M.

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att Ile	gga Gly	aaa Lys 35	agg Arg	agg Arg	cac His	ccc Pro	aaa Lys 40	aag Lys	ctg Leu	acc Thr	ccg Pro	tta Leu 45	gcc Ala	tat Tyr	aag Lys	144
cag Gln	ttt Phe 50	att Ile	ccc Pro	aat Asn	gtg Val	gca Ala 55	gag Glu	aag Lys	acc Thr	cta Leu	999 Gly 60	gcc Ala	agt Ser	gga Gly	aga Arg	192
tat Tyr 65	gaa Glu	ggg Gly	aag Lys	atc Ile	aca Thr 70	aga Arg	aac Asn	tcc Ser	gag Glu	aga Arg 75	ttt Phe	aaa Lys	gaa Glu	cta Leu	acc Thr 80	240
cca Pro	aat Asn	tac Tyr	aac Asn	cct Pro 85	gac Asp	att Ile	att Ile	ttt Phe	aag Lys 90	gat Asp	gaa Glu	gag Glu	aac Asn	acg Thr 95	gga Gly	288
gct Ala	gac Asp	aga Arg	ctg Leu 100	atg Met	act Thr	cag Gln	cgc Arg	tgc Cys 105	aag Lys	gac Asp	aag Lys	ctg Leu	aat Asn 110	gcc Ala	ctg Leu	336
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tac Tyr	gga Gly	atg Met	ctg Leu	gcc Ala 165	Arg	ctc Leu	gcc Ala	gtc Val	gag Glu 170	Ala	ggc Gly	ttc Phe	gac Asp	tgg Trp 175	gtc Val	528
tac Tyr	tac Tyr	gag Glu	tcc Ser 180	Lys	gcg Ala	cac His	ato Ile	cac His	Cys	tcc Ser	gto Val	aaa Lys	gca Ala 190	Glü	aac Asn	576
tca Ser	gtg Val	gca Ala 195	a Ala	g aaa Lys	tca Ser	gga	gg0 Gly 200	/ Cys	tto Phe	cct Pro	ggo Gly	tca Ser 205	Ala	aca Thr	gtg Val	624
cac	cto Lev	ı Glı	g cat ı His	gga Gly	ggc Gly	acc Thr	Lys	g ctg s Lei	g gtg ı Val	g aag Lys	gad Asp 220) Le	g ago 1 Sei	c cct	gly ggg	672

gac Asp 225	Arg	gtg Val	g ctg . Leu	gct Ala	gct Ala 230	Asp	gcg Ala	gac Asp	ggc Gly	cgg Arg 235	Leu	ctc Leu	tac Tyr	agt Ser	gac Asp 240	720
ttc Phe	ctc Leu	acc Thr	ttc Phe	ctc Leu 245	Asp	cgg Arg	atg Met	gac Asp	agc Ser 250	Ser	cga Arg	aag Lys	ctc Leu	ttc Phe 255		768
gtc Val	atc Ile	gag Glu	acg Thr 260	cgg Arg	cag Gln	ccc Pro	cgg Arg	gcc Ala 265	cgg Arg	ctg Leu	cta Leu	ctg Leu	acg Thr 270	gcg Ala	gcc Ala	816
cac His	ctg Leu	ctc Leu 275	ttt Phe	gtg Val	gcc Ala	ccc Pro	cag Gln 280	cac His	aac Asn	cag Gln	tcg Ser	gag Glu 285	gcc Ala	aca Thr	ggg Gly	864
tcc Ser	acc Thr 290	agt Ser	ggc Gly	cag Gln	gcg Ala	ctc Leu 295	ttc Phe	gcc Ala	agc Ser	aac Asn	gtg Val 300	aag Lys	cct Pro	ggc Gly	caa Gln	912
cgt Arg 305	gtc Val	tat Tyr	gtg Val	ctg Leu	ggc Gly 310	gag Glu	ggc Gly	Gly	cag Gln	cag Gln 315	ctg Leu	ctg Leu	ccg Pro	gcg Ala	tct Ser 320	960
gtc Val	cac His	agc Ser	gtc Val	tca Ser 325	ttg Leu	cgg Arg	gag Glu	gag Glu	gcg Ala 330	tcc Ser	gga Gly	gcc Ala	tac Tyr	gcc Ala 335	cca Pro	1008
ctc Leu	acc Thr	gcc Ala	cag Gln 340	ggc Gly	acc Thr	atc Ile	ctc Leu	atc Ile 345	aac Asn	cgg Arg	gtg Val	ttg Leu	gcc Ala 350	tcc Ser	tgc Cys	1056
tac Tyr	gcc Ala	gtc Val 355	atc Ile	gag Glu	gag Glu	cac His	agt Ser 360	tgg Trp	gcc Ala	cat His	tgg Trp	gcc Ala 365	ttc Phe	gca Ala	cca Pro	1104
ttc Phe	cgc Arg 370	ttg Leu	gct Ala	cag Gln	ggg ggg	ctg Leu 375	ctg Leu	gcc Ala	gcc Ala	ctc Leu	tgc Cys 380	cca Pro	gat Asp	gly ggg	gcc Ala	1152
atc Ile 385	cct Pro	act Thr	gcc Ala	gcc Ala	acc Thr 390	acc Thr	acc Thr	act Thr	ggc Gly	atc Ile 395	cat His	tgg Trp	tac Tyr	tca Ser	cgg Arg 400	1200
ctc Leu	ctc Leu	tac Tyr	cgc Arg	atc Ile 405	ggc Gly	agc Ser	tgg Trp	gtg Val	ctg Leu 410	gat Asp	ggt Gly	gac Asp	gcg Ala	ctg Leu 415	cat His	1248
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		. 501	20)	ser	Cys	g GIA	Pro 25	2 O GIA	y Arg	g Gly	y Pro	o Va]	l Gly O	c cgg y Arg	96			
9		35	Vai	g cgc . Arg	пув	GIN	40	vai	. Pro) Leu	ı Leu	u Tyr 45	r Lys 5	s Gln	1 Phe	144			
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5			100	gag Glu	Arg	Cys	ьуѕ	105	Arg	Val	Asn	Ala	110	Ala	Ile	336			
		115	ASII	atg Met	ırp	PIO	120	Val	Arg	Leu	Arg	Val 125	Thr	Glu	Gly	384			
₽	130	Olu 1	ASP .	ggc (nis	135	Ala	Gin .	Asp	Ser	Leu 140	His	Tyr	Glu	Gly	432			
145		Deu P	ASP .		150	int	ser /	Asp A	Arg .	Asp 155	Arg	Asn	Lys	Tyr	Gly 160	480			
		····	arg :	cta o Leu <i>I</i> 165	AIA \	Val (GIU A	Ala (170	Phe	Asp	Trp	Val	Tyr 175	Tyr	528			
		1	180	cac a His I	iie r	nis v	vai s	ser (185	val 1	Lys .	Ala	Asp	Asn 190	Ser	Leu	576			
gcg g Ala V		cga g Arg A 195	ycc ç	gga g Gly G	ıgc t }lγ (-ys P	ttt c Phe F 200	eg ç Pro (jga a ∃ly i	aat (Asn)	Ala '	acg Thr 205	gtg Val	cgc Arg	ttg Leu	624			

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		aag Lys						672
		gca Ala 230						720
		gat Asp						768
		ccg Pro						816
		gly aaa						864
		tta Leu						912
		ccg Pro 310						960
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aag gac cgt ctg aac tca ctg gcc atc tct gtc atg aac cag tgg cct 14 Lys Asp Arg Leu Asn Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro 45	:4 ·
ggt gtg aaa ctg cgg gtg acc gaa ggc tgg gat gaa gat ggc cat cac 19 Gly Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His 50 55 60	∋ 2
tca gag gag tct tta cac tat gag ggc cgc gcg gtg gat atc acc acc 24 Ser Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr 65 70 75 80	40
tca gac cgt gac cga aat aag tat gga ctg ctg gcg cgc tta gca gtg 2 Ser Asp Arg Asp Arg Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val 85 90 95	88
gag gcc ggc ttc gac tgg gtg tat tac gag tcc aag gcc cac gtg cat 3 Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Val His 100 105	36
tgc tct gtc aag tct gag cat tcg gcc gct gcc aag aca ggt ggc tgc 3 Cys Ser Val Lys Ser Glu His Ser Ala Ala Ala Lys Thr Gly Gly Cys 115 120 125	384
ttt cct gcc gga gcc cag gtg cgc cta gag aac ggg gag cgt gtg gcc Phe Pro Ala Gly Ala Gln Val Arg Leu Glu Asn Gly Glu Arg Val Ala 130 140	432
ctg tca gct gta aag cca gga gac cgg gtg ctg gcc atg ggg gag gat Leu Ser Ala Val Lys Pro Gly Asp Arg Val Leu Ala Met Gly Glu Asp 145 150 155	480
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aac cgg ctg aga gct ttc cag gtc atc gag act cag gat cct ccg cgt Asn Arg Leu Arg Ala Phe Gln Val Ile Glu Thr Gln Asp Pro Pro Arg 180 185 190	576
cgg ctg gcg ctc acg cct gcc cac ctg ctc ttc att gcg gac aat cat Arg Leu Ala Leu Thr Pro Ala His Leu Leu Phe Ile Ala Asp Asn His 195 200 205	624
aca gaa cca gca gcc cac ttc cgg gcc aca ttt gcc agc cat gtg caa Thr Glu Pro Ala Ala His Phe Arg Ala Thr Phe Ala Ser His Val Gln	672

210 215 220

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ctc Leu	aca Thr	agg Arg	cat His 260	Gly	aca Thr	ctt Leu	gtg Val	gtg Val 265	gag Glu	gat Asp	gtg Val	gtg Val	gcc Ala 270	tcc Ser	tgc Cys	816
ttt Phe	gca Ala	gct Ala 275	gtg Val	gct Ala	gac Asp	cac His	cat His 280	ctg Leu	gct Ala	cag Gln	ttg Leu	gcc Ala 285	ttc Phe	tgg Trp	ccc Pro	864
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cta Leu	gaa Glu	gag Glu	agc Ser	acc Thr 325	ttc Phe	cat His	cca Pro	ctg Leu	ggc Gly 330	atg Met	tct Ser	gly ggg	gca Ala	gga Gly 335	agc Ser	1008
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tac Tyr	aac Asn	ccc Pro	gac Asp	atc Ile 85	ata Ile	ttt Phe	aag Lys	gat Asp	gag Glu 90	gaa Glu	aac Asn	acg Thr	gga Gly	gca Ala 95	gac Asp	288
cgg Arg	ctg Leu	atg Met	act Thr 100	cag Gln	agg Arg	tgc Cys	aaa Lys	gac Asp 105	aag Lys	tta Leu	aat Asn	gcc Ala	ttg Leu 110	gcc Ala	atc Ile	336
tct Ser	gtg Val	atg Met 115	aac Asn	cag Gln	tgg Trp	cct Pro	gga Gly 120	gtg Val	aag Lys	ctg Leu	cga Arg	gtg Val 125	acc Thr	gag Glu	ggc Gly	384
tgg Trp	gat Asp 130	gag Glu	gac Asp	ggc Gly	cat His	cat His 135	tca Ser	gag Glu	gag Glu	tct Ser	cta Leu 140	cac His	tat Tyr	gag Glu	ggt Gly	432
cga Arg 145	gca Ala	gtg Val	gac Asp	atc Ile	acc Thr 150	acg Thr	tcc Ser	gac Asp	cgg Arg	gac Asp 155	cgc Arg	agc Ser	aag Lys	tac Tyr	ggc Gly 160	480
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cac ggc acc His Gly Th												
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ttg gtg gtg Leu Val Val												

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							aga Arg									240
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						_	aag Lys	_	_				_	_		672
Leu 225	Ala	Ala	Asp	Ser	Ala 230	Gly	aac Asn	Leu	Val	Phe 235	Ser	Asp	Phe	Ile	Met 240	720
							acg Thr									768

acg caa gaa ccc gtt gaa aag atc acc ctc acc gcc gct cac ctc ctt Thr Gln Glu Pro Val Glu Lys Ile Thr Leu Thr Ala Ala His Leu Leu 260 265 270	816											
ttt gtc ctc gac aac tca acg gaa gat ctc cac acc atg acc gcc gcg Phe Val Leu Asp Asn Ser Thr Glu Asp Leu His Thr Met Thr Ala Ala 275 280 285	864											
tat gcc agc agt gtc aga gcc gga caa aag gtg atg gtt gtt gat gat Tyr Ala Ser Ser Val Arg Ala Gly Gln Lys Val Met Val Val Asp Asp 290 295 300	912											
agc ggt cag ctt aaa tct gtc atc gtg cag cgg ata tac acg gag gag Ser Gly Gln Leu Lys Ser Val Ile Val Gln Arg Ile Tyr Thr Glu Glu 305 310 315 320	960											
cag cgg ggc tcg ttc gca cca gtg act gca cat ggg acc att gtg gtc Gln Arg Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile Val Val 325 330 335	1008											
gac aga ata ctg gcg tcc tgt tac gcc gta ata gag gac cag ggg ctt Asp Arg Ile Leu Ala Ser Cys Tyr Ala Val Ile Glu Asp Gln Gly Leu 340 345 350	1056											
gcg cat ttg gcc ttc gcg ccc gcc agg ctc tat tat tac gtg tca tca Ala His Leu Ala Phe Ala Pro Ala Arg Leu Tyr Tyr Tyr Val Ser Ser 355 360 365	1104											
ttc ctg ttc ccc caa aac tcc agc agt cgg tcc aat gcg act tta caa Phe Leu Phe Pro Gln Asn Ser Ser Ser Arg Ser Asn Ala Thr Leu Gln 370 375 380	1152											
cag gag ggg gtc cac tgg tac tcc agg ctc ctg tat caa atg gga acg Gln Glu Gly Val His Trp Tyr Ser Arg Leu Leu Tyr Gln Met Gly Thr 385 390 395 400	1200											
tgg ctt ttg gac agc aac atg ctt cat cct ttg ggg atg tca gta aac Trp Leu Leu Asp Ser Asn Met Leu His Pro Leu Gly Met Ser Val Asn 405 410 415	1248											
tca agc tga Ser Ser	1257											
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195 200 205

		ctg Leu							672
		cag Gln 230							720
		gac Asp							768
		gag Glu							816
		aac Asn							864
		cct Pro							912
		cgc Arg 310							960
		cgg Arg	_	_	_		_		1008
		gcg Ala							1056
		cgg Arg							1104
		cac His							1152
		ctg Leu 390							1200
		cgc Arg							1248
		gac Asp							1296

					ctg Leu						gac Asp	1344
					ccg Pro							1392
					999 Gly 470							1425
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cgg		ctc			cag Gln							48
					cag Gln							96
					ggc Gly							144
					atc Ile							192
					ttg Leu 70							240
					cac His							288
					ggc Gly							336
					cgt Arg							384
					gly 999							432

130 135 140

ctc att ttc ctg gac cgc gag ccc cac agg ctg aga gcc ttc cag Leu Ile Phe Leu Asp Arg Glu Pro His Arg Leu Arg Ala Phe Gln 145 ' 150 155	_											
atc gag act cag gac ccc cca cgc cgc ctg gca ctc aca ccc gct Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr Pro Ala 165 170 175												
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gcc aca ttt gcc agc cac gtg cag cct ggc cag tac gtg ctg gtg Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val Leu Val 195 200 205												
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gtg gcc ctc ggg gcc tac gcc ccg ctc aca aag cat ggg aca ctg Val Ala Leu Gly Ala Tyr Ala Pro Leu Thr Lys His Gly Thr Leu 225 230 235												
gtg gag gat gtg gtg gca tcc tgc ttc gcg gcc gtg gct gac cac Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala Asp His 245 250 255												
ctg gct cag ttg gcc ttc tgg ccc ctg aga ctc ttt cac agc ttg Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe His Ser Leu 260 265 270												
tgg ggc agc tgg acc ccg ggg gag ggt gtg cat tgg tac ccc cag Trp Gly Ser Trp Thr Pro Gly Glu Gly Val His Trp Tyr Pro Gln 275 280 285												
ctc tac cgc ctg ggg cgt ctc ctg cta gaa gag ggc agc ttc cac Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Gly Ser Phe His 290 295 300												
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<400> 34 Met Val Glu Met Leu Leu Thr Arg Ile Leu Leu Val Gly Phe	Ile											
Cys Ala Leu Leu Val Ser Ser Gly Leu Thr Cys Gly Pro Gly Arg 20 25 30	Gly											

Ile Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
35 40 45

Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg
50 55 60

Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr 65 70 75 80

Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly 85 90 95

Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu 100 105 110

Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr 115 120 125

Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr 130 135 140

Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys 145 150 155 160

Tyr Gly Met Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val 165 170 175

Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn 180 185 190

Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val 195 200 205

His Leu Glu His Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly 210 215 220

Asp Arg Val Leu Ala Ala Asp Ala Asp Gly Arg Leu Leu Tyr Ser Asp 225 230 235 240

Phe Leu Thr Phe Leu Asp Arg Met Asp Ser Ser Arg Lys Leu Phe Tyr 245 250 255

Val Ile Glu Thr Arg Gln Pro Arg Ala Arg Leu Leu Thr Ala Ala 260 265 270

His Leu Leu Phe Val Ala Pro Gln His Asn Gln Ser Glu Ala Thr Gly 275 280 285

Ser Thr Ser Gly Gln Ala Leu Phe Ala Ser Asn Val Lys Pro Gly Gln 290 295 300

Arg Val Tyr Val Leu Gly Glu Gly Gly Gln Gln Leu Leu Pro Ala Ser 305 310 315 320

Val His Ser Val Ser Leu Arg Glu Glu Ala Ser Gly Ala Tyr Ala Pro 325 330 335 Leu Thr Ala Gln Gly Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys 340 345 350

Tyr Ala Val Ile Glu Glu His Ser Trp Ala His Trp Ala Phe Ala Pro 355 360 365

Phe Arg Leu Ala Gln Gly Leu Leu Ala Ala Leu Cys Pro Asp Gly Ala 370 380

Ile Pro Thr Ala Ala Thr Thr Thr Gly Ile His Trp Tyr Ser Arg
385 390 395 400

Leu Leu Tyr Arg Ile Gly Ser Trp Val Leu Asp Gly Asp Ala Leu His
405 410 415

Pro Leu Gly Met Val Ala Pro Ala Ser 420 425

<210> 35

<211> 396

<212> PRT

<213> Mus musculus

<400> 35

Met Ala Leu Pro Ala Ser Leu Leu Pro Leu Cys Cys Leu Ala Leu Leu 1 5 10 15

Ala Leu Ser Ala Gln Ser Cys Gly Pro Gly Arg Gly Pro Val Gly Arg
20 25 30

Arg Arg Tyr Val Arg Lys Gln Leu Val Pro Leu Leu Tyr Lys Gln Phe 35 40 45

Val Pro Ser Met Pro Glu Arg Thr Leu Gly Ala Ser Gly Pro Ala Glu 50 55 60

Gly Arg Val Thr Arg Gly Ser Glu Arg Phe Arg Asp Leu Val Pro Asn 65 70 75 80

Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Ser Gly Ala Asp 85 90 95

Arg Leu Met Thr Glu Arg Cys Lys Glu Arg Val Asn Ala Leu Ala Ile 100 105 110

Ala Val Met Asn Met Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly
115 120 125

Trp Asp Glu Asp Gly His His Ala Gln Asp Ser Leu His Tyr Glu Gly
130 140

Arg Ala Leu Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly
145 150 155 160

Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr

165 170 175

Glu Ser Arg Asn His Ile His Val Ser Val Lys Ala Asp Asn Ser Leu 180 185 190

Ala Val Arg Ala Gly Gly Cys Phe Pro Gly Asn Ala Thr Val Arg Leu 195 200 205

Arg Ser Gly Glu Arg Lys Gly Leu Arg Glu Leu His Arg Gly Asp Trp 210 215 220

Val Leu Ala Ala Asp Ala Ala Gly Arg Val Val Pro Thr Pro Val Leu 225 230 235 240

Leu Phe Leu Asp Arg Asp Leu Gln Arg Arg Ala Ser Phe Val Ala Val 245 250 255

Glu Thr Glu Arg Pro Pro Arg Lys Leu Leu Leu Thr Pro Trp His Leu 260 265 270

Val Phe Ala Ala Arg Gly Pro Ala Pro Ala Pro Gly Asp Phe Ala Pro 275 280 285

Val Phe Ala Arg Arg Leu Arg Ala Gly Asp Ser Val Leu Ala Pro Gly
290 295 300

Gly Asp Ala Leu Gln Pro Ala Arg Val Ala Arg Val Ala Arg Glu Glu 305 310 315 320

Ala Val Gly Val Phe Ala Pro Leu Thr Ala His Gly Thr Leu Leu Val 325 330 335

Asn Asp Val Leu Ala Ser Cys Tyr Ala Val Leu Glu Ser His Gln Trp 340 345 350

Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala 355 360 365

Leu Leu Pro Gly Gly Ala Val Gln Pro Thr Gly Met His Trp Tyr Ser 370 375 380

Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Met Gly 385 390 395

<210> 36

<211> 336

<212> PRT

<213> Mus musculus

<400> 36

Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe 1 5 10 15

Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys
20 25 30

Lys Asp Arg Leu Asn Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro

35 40 45

Gly Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His 50 Ser Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Val His 105 Cys Ser Val Lys Ser Glu His Ser Ala Ala Ala Lys Thr Gly Gly Cys 120 Phe Pro Ala Gly Ala Gln Val Arg Leu Glu Asn Gly Glu Arg Val Ala Leu Ser Ala Val Lys Pro Gly Asp Arg Val Leu Ala Met Gly Glu Asp Gly Thr Pro Thr Phe Ser Asp Val Leu Ile Phe Leu Asp Arg Glu Pro Asn Arg Leu Arg Ala Phe Gln Val Ile Glu Thr Gln Asp Pro Pro Arg 180 185 Arg Leu Ala Leu Thr Pro Ala His Leu Leu Phe Ile Ala Asp Asn His 200 Thr Glu Pro Ala Ala His Phe Arg Ala Thr Phe Ala Ser His Val Gln 210 215 Pro Gly Gln Tyr Val Leu Val Ser Gly Val Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val Ser Thr His Val Ala Leu Gly Ser Tyr Ala Pro Leu Thr Arg His Gly Thr Leu Val Val Glu Asp Val Val Ala Ser Cys 260 Phe Ala Ala Val Ala Asp His His Leu Ala Gln Leu Ala Phe Trp Pro 280 Leu Arg Leu Phe Pro Ser Leu Ala Trp Gly Ser Trp Thr Pro Ser Glu 290 295 300 Gly Val His Trp Tyr Pro Gln Met Leu Tyr Arg Leu Gly Arg Leu Leu 305 Leu Glu Glu Ser Thr Phe His Pro Leu Gly Met Ser Gly Ala Gly Ser

330

325

<211> 437

<212> PRT

<213> Mus musculus

<400> 37

Met Leu Leu Leu Ala Arg Cys Phe Leu Val Ile Leu Ala Ser Ser 1 5 10 15

Leu Leu Val Cys Pro Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly 20 25 30

Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe
35 40 45

Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu
50 60

Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn 65 70 75 80

Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp 85 90 95

Arg Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile 100 105 110

Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly 115 120 125

Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly 130 135 140

Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly
145 150 155 160

Met Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr 165 170 175

Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val 180 185 190

Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val His Leu 195 200 205

Glu Gln Gly Gly Thr Lys Leu Val Lys Asp Leu Arg Pro Gly Asp Arg 210 215 220

Val Leu Ala Ala Asp Asp Gln Gly Arg Leu Leu Tyr Ser Asp Phe Leu 225 230 235 240

Thr Phe Leu Asp Arg Asp Glu Gly Ala Lys Lys Val Phe Tyr Val Ile 245 250 255

Glu Thr Leu Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu 260 265 270

Leu Phe Val Ala Pro His Asn Asp Ser Gly Pro Thr Pro Gly Pro Ser

275 280 285

Ala Leu Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val 290 295 300

Ala Glu Arg Gly Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser 305 310 315 320

Val Thr Leu Arg Glu Glu Glu Ala Gly Ala Tyr Ala Pro Leu Thr Ala 325 330 335

His Gly Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val 340 345 350

Ile Glu Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu 355 360 365

Ala His Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Gly Gly 370 375 380

Gly Gly Gly Ser Ile Pro Ala Ala Gln Ser Ala Thr Glu Ala Arg Gly 385 390 395 400

Ala Glu Pro Thr Ala Gly Ile His Trp Tyr Ser Gln Leu Leu Tyr His 405 410 415

Ile Gly Thr Trp Leu Leu Asp Ser Glu Thr Met His Pro Leu Gly Met
420 425 430

Ala Val Lys Ser Ser 435

<210> 38

<211> 418

<212> PRT

<213> Brachydanio rerio

<400> 38

Met Arg Leu Leu Thr Arg Val Leu Leu Val Ser Leu Leu Thr Leu Ser 1 5 10 15

Leu Val Val Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Tyr Gly Arg
20 25 30

Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile 35 40

Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly 50 60

Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr 65 70 75 80

Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg
85 90 95

Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser

100 105 110

Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp
115 120 125

Asp Glu Asp Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg 130 135 140

Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys Tyr Gly Thr 145 150 155 160

Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu 165 170 175

Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala 180 185 190

Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Leu Val Ser Leu Gln 195 200 205

Asp Gly Gln Lys Ala Val Lys Asp Leu Asn Pro Gly Asp Lys Val 210 215 220

Leu Ala Ala Asp Ser Ala Gly Asn Leu Val Phe Ser Asp Phe Ile Met 225 230 235 240

Phe Thr Asp Arg Asp Ser Thr Thr Arg Arg Val Phe Tyr Val Ile Glu 245 250 255

Thr Gln Glu Pro Val Glu Lys Ile Thr Leu Thr Ala Ala His Leu Leu 260 265 270

Phe Val Leu Asp Asn Ser Thr Glu Asp Leu His Thr Met Thr Ala Ala 275 280 285

Tyr Ala Ser Ser Val Arg Ala Gly Gln Lys Val Met Val Val Asp Asp 290 295 300

Ser Gly Gln Leu Lys Ser Val Ile Val Gln Arg Ile Tyr Thr Glu Glu 305 310 315 320

Gln Arg Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile Val Val 325 330 335

Asp Arg Ile Leu Ala Ser Cys Tyr Ala Val Ile Glu Asp Gln Gly Leu 340 345 350

Ala His Leu Ala Phe Ala Pro Ala Arg Leu Tyr Tyr Tyr Val Ser Ser 355 360 365

Phe Leu Phe Pro Gln Asn Ser Ser Ser Arg Ser Asn Ala Thr Leu Gln 370 375 380

Gln Glu Gly Val His Trp Tyr Ser Arg Leu Leu Tyr Gln Met Gly Thr 385 390 395 400

Trp Leu Leu Asp Ser Asn Met Leu His Pro Leu Gly Met Ser Val Asn

Ser Ser

<210> 39

<211> 475

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (463)

<223> Xaa=unknown amino acid

<400> 39

Met Leu Leu Leu Ala Arg Cys Leu Leu Val Leu Val Ser Ser Leu

1 5 10 15

Leu Val Cys Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly Lys
20 25 30

Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile 35 40 45

Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly 50 60

Lys Ile Ser Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr 65 70 75 80

Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg 85 90 95

Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile Ser 100 105 110

Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp 115 120 125

Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg 130 135 140

Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly Met 145 150 155 160

Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu 165 170 175

Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala 180 185 190

Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val His Leu Glu 195 200 205

Gln Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly Asp Arg Val 210 215 220 Leu Ala Ala Asp Asp Gln Gly Arg Leu Leu Tyr Ser Asp Phe Leu Thr 225 230 235 240

Phe Leu Asp Arg Asp Asp Gly Ala Lys Lys Val Phe Tyr Val Ile Glu 245 250 255

Thr Arg Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu Leu 260 265 270

Phe Val Ala Pro His Asn Asp Ser Ala Thr Gly Glu Pro Glu Ala Ser 275 280 285

Ser Gly Ser Gly Pro Pro Ser Gly Gly Ala Leu Gly Pro Arg Ala Leu 290 295 300

Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val Ala Glu 305 310 315 320

Arg Asp Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser Val Thr 325 330 335

Leu Ser Glu Glu Ala Ala Gly Ala Tyr Ala Pro Leu Thr Ala Gln Gly 340 345 350

Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val Ile Glu 355 360 365

Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu Ala His 370 380

Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Arg Gly Gly Asp 385 390 395 400

Ser Gly Gly Gly Asp Arg Gly Gly Gly Gly Arg Val Ala Leu Thr 405 410 415

Ala Pro Gly Ala Ala Asp Ala Pro Gly Ala Gly Ala Thr Ala Gly Ile 420 425 430

His Trp Tyr Ser Gln Leu Leu Tyr Gln Ile Gly Thr Trp Leu Leu Asp 435 440 445

Ser Glu Ala Leu His Pro Leu Gly Met Ala Val Lys Ser Ser Xaa Ser 450 455 460

Arg Gly Ala Gly Gly Gly Ala Arg Glu Gly Ala 465 470 475

<210> 40

<211> 312

<212> PRT

<213> Homo sapiens

<400> 40

Arg Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn Ser Leu Ala 1 5 10 15

Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu 25 Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr 70 Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser Glu His Ser Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala Gln Val Arg 100 105 Leu Glu Ser Gly Ala Arg Val Ala Leu Ser Ala Val Arg Pro Gly Asp 120 115 125 Arg Val Leu Ala Met Gly Glu Asp Gly Ser Pro Thr Phe Ser Asp Val 135 Leu Ile Phe Leu Asp Arg Glu Pro His Arg Leu Arg Ala Phe Gln Val 150 155 Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr Pro Ala His 170 Leu Leu Phe Thr Ala Asp Asn His Thr Glu Pro Ala Ala Arg Phe Arg 180 185 190 Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val Leu Val Ala 200 Gly Val Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val Ser Thr His 215 220 Val Ala Leu Gly Ala Tyr Ala Pro Leu Thr Lys His Gly Thr Leu Val 230 235 Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala Asp His His 245 250 Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe His Ser Leu Ala 260 265 Trp Gly Ser Trp Thr Pro Gly Glu Gly Val His Trp Tyr Pro Gln Leu 275 280 Leu Tyr Arg Leu Gly Arg Leu Leu Glu Glu Gly Ser Phe His Pro 295 Leu Gly Met Ser Gly Ala Gly Ser <210> 41 <211> 167 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: General hedgehog polypeptide formula <220> <221> SITE <222> (7) <223> Xaa=Gly, Ala, Val, Leu, Ile, Pro, Phe, or Tyr <220> <221> SITE <222> (8) <223> Xaa=Gly, Ala, Val, Leu, or Ile

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<221> SITE
<222> (9)
<223> Xaa=Gly, Ala, Val, Leu, Ile, Lys, His, or Arg
<220>
<221> SITE
<222> (12)
<223> Xaa=Lys, Arg or His
<220>
<221> SITE
<222> (13)
<223> Xaa=Phe, Trp, Tyr, or an amino acid gap
<220>
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<222> (14)
<223> Xaa=Gly, Ala, Val, Leu, Ile, or an amino acid gap
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<222> (17)
<223> Xaa=Asn, Gln, His, Arg, or Lys
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<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr
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<222> (22)
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<223> Xaa=Ser, Thr, Gln, or Asn
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<222> (30)
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<222> (46)
<223> Xaa=Thr or Ser
<220>
<221> SITE
<222> (48)
<223> Xaa=Ly, Ala, Val, Leu, Ile, Asn, or Gln
<220>
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<223> Xaa=Asp or Glu
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<223> Xaa=Ser or Thr
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<223> Xaa=Glu, Asp, Gln, or Asn
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<220>
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<222> (84)
<223> Xaa=Arg, His or Lys
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<222> (85)
<223> Xaa=Gly, Ala, Val, Leu, or Ile
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<223> Xaa=Gly, Ala, Val, Leu, Ile, Thr, or Ser
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<222> (95)
<223> Xaa=Met, Cys, Gln, Asn, Arg, Lys, or His
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<222> (100)
<223> Xaa=Arg, His or Lys
<220>
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Xaa Leu Xaa Pro Leu Xaa Tyr Lys Gln Phe Xaa Pro Xaa Xaa Xaa Glu
                                  25
Xaa Thr Leu Gly Ala Ser Gly Xaa Xaa Glu Gly Xaa Xaa Xaa Arg Xaa
Ser Glu Arg Phe Xaa Xaa Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile
                         55
                                              60
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Phe Lys Asp Glu Glu Asn Xaa Gly Ala Asp Arg Leu Met Thr Xaa Arg 75 Tys Lys Xaa Xaa Xaa Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp 85 90 Pro Gly Val Xaa Leu Arg Val Thr Glu Gly Xaa Asp Glu Asp Gly His 105 His Xaa Xaa Xaa Ser Leu His Tyr Glu Gly Arg Ala Xaa Asp Ile Thr Thr Ser Asp Arg Asp Xaa Xaa Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala 130 135 Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Xaa Xaa His Xaa 155 His Xaa Ser Val Lys Xaa Xaa 165 <210> 42 <211> 165 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: General Shh polypeptide formula <220> <221> SITE <222> (7) <223> Xaa=Gly, Ala, Val, Leu, Ile, Phe, Tyr, or Trp <220> <221> SITE <222> (9) <223> Xaa=Arg, His or Lys <220> <221> SITE <222> (44) <223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr <220> <221> SITE <222> (85) <223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr <220> <221> SITE <222> (93)

<223> Xaa=Lys, Arg, His, Asn, or Gln

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Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr
Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Xaa Arg Asn Ser Glu
                                                  45
Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys
Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys
                                         75
Asp Lys Leu Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp Pro Gly
Val Xaa Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Xaa
Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser
        115
                            120
Asp Arg Asp Xaa Ser Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala Val Glu
Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys
                    150
                                        155
Ser Val Lys Ala Glu
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Lor 165

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